Serial No.: <u>10/076,674</u> Docket No.: <u>1004263.156US (1151-4172)</u>

## AMENDMENTS TO CLAIMS

The listing of claims replaces all prior versions of claims in the application.

#### Listing of Claims

 (Previously Presented) A stabilized immunostimulatory microparticulate complex comprising a cationic peptide immunogen wherein the peptide immunogen comprises a target B cell antigen or a CTL epitope and a T helper cell epitope and

an anionic CpG oligonucleotide

wherein the cationic peptide immunogen has a net positive charge at a pH in the range of 5.0 to 8.0 calculated by assigning a +1 charge for each lysine (K), arginine (R) or histidine (H), a -1 charge for each aspartic acid (D) or glutamic acid (E) and a charge of 0 for all other amino acids in the peptide immunogen and

wherein the anionic CpG oligonucleotide has a net negative charge at a pH in the range of 5.0-8.0 and is a single-stranded DNA comprising 8 to 64 nucleotide bases with a repeat of a cytosine-guanidine motif and the number of repeats of the CpG motif is in the range of 1 to 10, and

wherein the cationic peptide immunogen: CpG oligonucleotide charge ratio ranges from 8:1 to 1:2 and

wherein the microparticulate complex is a precipitate with an average particle size of about 22.5 microns or less.

### 2-3. (Cancelled)

- (Previously presented) The immunostimulatory microparticulate complex of claim 1, wherein the cationic peptide immunogen is a mixture of synthetic peptide immunogens.
- (Previously presented) The immunostimulatory microparticulate complex of claim 1, wherein the net positive charge of the cationic peptide immunogen is at least +2.
- (Previously presented) The immunostimulatory microparticulate complex of claim 4, wherein the average net positive charge of the mixture of synthetic peptide immunogens is at least +2.

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 (Previously presented) The immunostimulatory microparticulate complex of claim 5 or 6, wherein the net negative charge of the anionic oligonucleotide is at least -2.

- (Previously presented) The immunostimulatory microparticulate complex of claim 1, wherein the CpG oligonucleotide is a single-stranded DNA molecules with 18-48 nucleotide bases and the number of repeats of CpG motif therein in the range of 3 to 8.
- 9. (Previously presented) The immunostimulatory microparticulate complex of claim 1, wherein the CpG oligonucleotide has the formula:  $5' X'CGX^2 3'$  wherein C and G are unmethylated; and  $X^1$  is selected from the group consisting of A (adenine), G (quanine) and T (thymine); and  $X^2$  is C (cytosine) or T (thymine).

# 10.-11. (Cancelled)

- 12. (Previously presented) The immunostimulatory microparticulate complex of claim 1, wherein CpG oligonucleotide is selected from a group consisting of 5' TCG TCG TTT TGT CGT TTT GTC GTT TTG TCG TT 3' (CpG1) SEQ ID NO: 1, a 32 base length oligomer, and 5'nTC GTC GTT TTG TCG TTT TGT CGT T 3' (CpG2) SEQ ID NO: 2, a 24 base length oligomer plus an phosphorothioate group designated as n.
- 13. (Previously presented) The immunostimulatory microparticulate complex of claim 12, wherein CpG oligonucleotide is 5' TCG TCG TTT TGT CGT TTT GTC GTT TTG TCG TT 3' (CpG1) SEQ ID NO: 1.

#### 14.-17. (Cancelled)

- 18. (Previously presented) The immunostimulatory microparticulate complex of claim 12, wherein the cationic peptide immunogen is a synthetic peptide conjugated to a T helper cell epitope.
- 19. (Previously presented) The immunostimulatory microparticulate complex of claim 18, wherein the cationic immunogen is selected from the group consisting of SEO ID NO: 7. 8 and 9 and a mixture thereof.

# 20. -75. (Cancelled)

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76. (Previously presented) The immunostimulatory microparticulate complex of claim 1, wherein the cationic peptide immunogen:CpG oligonucleotide charge ratio ranges from 4:1 to 1:1.

- 77. (Previously presented) The immunostimulatory microparticulate complex of claim 1, wherein the microparticulate complex is a precipitate with an average particle size of about 10 microns or less.
- 78. (Previously presented) A stabilized immunostimulatory microparticulate complex comprising a cationic peptide immunogen wherein the peptide immunogen comprises a target B cell antigen or a CTL epitope and a T helper cell epitope and an anionic CpG oligonucleotide

wherein the cationic peptide immunogen has a net positive charge at a pH in the range of 5.0 to 8.0 calculated by assigning a +1 charge for each lysine (K), arginine (R) or histidine (H), a -1 charge for each aspartic acid (D) or glutamic acid (E) and a charge of 0 for all other amino acids in the peptide immunogen and

wherein the anionic CpG oligonucleotide has a net negative charge at a pH in the range of 5.0-8.0 and is a single-stranded DNA comprising 8 to 64 nucleotide bases with a repeat of a cytosine-guanidine motif and the number of repeats of the CpG motif is in the range of 1 to 10, and

wherein the cationic peptide immunogen:CpG oligonucleotide charge ratio ranges from 8:1 to 1:2 and

wherein the microparticulate complex is formed by combining the CpG oligonucleotide to the cationic peptide immunogen, or vice versa, in a dropwise manner to form a precipitate with an average particle size of about 22.5 microns or less. Docket No.: 1004263.156US (1151-4172)

79. (Previously presented) The immunostimulatory microparticulate complex of claim 78, wherein the cationic peptide immunogen is a mixture of synthetic peptide immunogens.

- 80. (Previously presented) The immunostimulatory microparticulate complex of claim 78, wherein the net positive charge of the cationic peotide immunogen is at least +2.
- 81. (Previously presented) The immunostimulatory microparticulate complex of claim 79, wherein the average net positive charge of the mixture of synthetic peptide immunogens is at least +2.
- 82. (Previously presented) The immunostimulatory microparticulate complex of claim 80 or 81, wherein the net negative charge of the anionic oligonucleotide is at least -2.
- 83. (Previously presented)

  The immunostimulatory microparticulate complex of claim 78, wherein the CpG oligonucleotide is a single-stranded DNA molecules with 18-48 nucleotide bases and the number of repeats of CpG motif
- 84. (Previously presented) The immunostimulatory microparticulate complex of claim 78, wherein the CpG oligonucleotide has the formula: 5' X1CGX2 3' wherein C and G are unmethylated; and X1 is selected from the group consisting of A (adenine), G (guanine) and T (thymine); and X2 is C (cytosine) or T (thymine).
- 85. (Previously presented) The immunostimulatory microparticulate complex of claim 78, wherein CpG oligonucleotide is selected from a group consisting of 5' TCG TCG TTT TGT CGT TTT GTC GTT TTG TCG TT 3' (CpG1) SEQ ID NO: 1, a 32 base length oligomer, and 5'nTC GTC GTT TTG TCG TTT TGT CGT T 3' (CpG2) SEQ ID NO: 2, a 24 base length oligomer plus an phosphorothicate group designated as n.
- 86 (Previously presented) The immunostimulatory microparticulate complex of claim 85, wherein CpG oligonucleotide is 5' TCG TCG TTT TGT CGT TTT GTC GTT TTG TCG TT 3' (CpG1) SEQ ID NO: 1.

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87. (Previously presented) The immunostimulatory microparticulate complex of claim 85, wherein the cationic peptide immunogen is a synthetic peptide conjugated to a T helper cell epitope.

- 88. (Previously presented) The immunostimulatory microparticulate complex of claim 87, wherein the cationic immunogen is selected from the group consisting of SEQ ID NO: 7. 8 and 9 and a mixture thereof.
- (Previously presented) The immunostimulatory microparticulate complex of claim 78, wherein the cationic peptide immunogen:CpG oligonucleotide charge ratio ranges from 4:1 to 1:1.
- 90. (Previously presented) The immunostimulatory microparticulate complex of claim 78, wherein the microparticulate complex is a precipitate with an average particle size of about 10 microns or less.